CLAIMS

We claim:

1. A targeting construct comprising:

(a) a first polynucleotide sequence homologous to a anaphylatoxin C3a receptor gene;

(b) a second polynucleotide sequence homologous to the anaphylatoxin C3a receptor gene; and

(c) a selectable marker.

2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.

3. A method of producing a targeting construct, the method comprising:

(a) providing a first polynucleotide sequence homologous to a anaphylatoxin C3a receptor gene;

(b) providing a second polynucleotide sequence homologous to the anaphylatoxin C3a receptor;

(c) providing a selectable marker; and

(d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.

4. A method of producing a targeting construct, the method comprising:

(a) providing a polynucleotide comprising a first sequence homologous to a first region of a anaphylatoxin C3a receptor gene and a second sequence homologous to a second receptor of an anaphylatoxin C3a receptor gene;

(b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.

5. A cell comprising a disruption in an anaphylatoxin C3a receptor gene.

6. The cell of claim 5, wherein the cell is a murine cell.

7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.

8. A non-human transgenic animal comprising a disruption in an anaphylatoxin C3a receptor gene.

9. A cell derived from the non-human transgenic animal of claim 8.

10. A method of producing a transgenic mouse comprising a disruption in a anaphylatoxin C3a receptor gene, the method comprising:

(a) introducing the targeting construct of claim 1 into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a anaphylatoxin C3a receptor, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a anaphylatoxin C3a receptor gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression of anaphylatoxin C3a receptor in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a anaphylatoxin C3a receptor, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a anaphylatoxin C3a receptor gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the function of the disrupted anaphylatoxin C3a receptor gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of anaphylatoxin C3a receptor, the method comprising:

(a) providing a cell comprising a disruption in a anaphylatoxin C3a receptor gene;

(b) contacting the cell with an agent; and

(c) determining whether expression of the anaphylatoxin C3a receptor is modulated.

14. A method of identifying an agent that modulates the function of a anaphylatoxin C3a receptor gene, the method comprising:

(a) providing a cell comprising a disruption in a anaphylatoxin C3a receptor gene;

(b) contacting the cell with an agent; and

(c) determining whether the function of the anaphylatoxin C3a receptor gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in an anaphylatoxin C3a receptor gene, wherein the transgenic mouse exhibits an abnormality of the thymus.

18. The transgenic mouse of claim 17, wherein the thymus abnormality is reduced weight of the thymus relative to a wild-type mouse.

19. The transgenic mouse of claim 17, wherein the thymus abnormality is reduced size of the thymus relative to a wild-type mouse.

20. The transgenic mouse of claim 17, wherein the thymus abnormality is a reduced thymus to body weight ratio relative to a wild-type mouse.

21. A transgenic mouse comprising a disruption in an anaphylatoxin C3a receptor gene, wherein the transgenic mouse exhibits an increased susceptibility to seizure.

22. The transgenic mouse of claim 21, wherein the mouse exhibits seizure-like responses at a lower dose of Metrazol relative to a wild-type mouse.

23. A transgenic mouse comprising a disruption in an anaphylatoxin C3a receptor gene, wherein the transgenic mouse exhibits a stimulus processing deficit relative to a wild-type mouse.

24. The transgenic mouse of claim 23, wherein the stimulus processing deficit is similar to that observed in schizophrenia.

25. The transgenic mouse of claim 23, wherein the mouse exhibits decreased prepulse inhibition relative to a wild-type mouse.

26. A method of producing a transgenic mouse comprising a disruption in a anaphylatoxin C3a receptor gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: an abnormality of the thymus, an increased susceptibility to seizure, or a stimulus processing deficit, the method comprising:

(a) introducing a anaphylatoxin C3a receptor gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in an anaphylatoxin C3a receptor gene.

27. A cell derived from the transgenic mouse of claim 17 or claim 26.

28. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a anaphylatoxin C3a receptor gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a anaphylatoxin C3a receptor gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: an abnormality of the thymus, an increased susceptibility to seizure, or a stimulus processing deficit.

29. A method of identifying an agent that modulates anaphylatoxin C3a receptor expression, the method comprising:

(a) administering an agent to the transgenic mouse comprising a disruption in a anaphylatoxin C3a receptor gene; and

(b) determining whether the agent modulates anaphylatoxin C3a receptor expression in the transgenic mouse, wherein the agent has an effect on at least one of the following behaviors: susceptibility to seizure and stimulus processing.

30. A method of identifying an agent that modulates a behavior associated with a disruption in a anaphylatoxin C3a receptor gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a anaphylatoxin C3a receptor gene; and

(b) determining whether the agent modulates at least one of the following behaviors: susceptibility to seizure and stimulus processing.

31. A method of identifying an agent that modulates anaphylatoxin C3a receptor gene function, the method comprising:

(a) providing a cell comprising a disruption in a anaphylatoxin C3a receptor gene;

(b) contacting the cell with an agent; and

(c) determining whether the agent modulates anaphylatoxin C3a receptor gene

function, wherein the agent modulates a phenotype associated with a disruption in an anaphylatoxin C3a receptor gene.

32. The method of claim 31, wherein the phenotype comprises at least one of the following an abnormality of the thymus, an increased susceptibility to seizure, and a stimulus processing deficit.

33. An agent identified by the method of claim 28, claim 29, claim 30, or claim 31.